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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,172	02/12/2004	Stephen D. Wolpe	1331-413	4014

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/776,172	WOLPE ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-46 and 53-97* is/are pending in the application.

4a) Of the above claim(s) *9-46, 53-65 and 69-92* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-68 and 93-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5-0-0

DETAILED ACTION

1. Applicant's amendment, filed 06/21/05 is acknowledged.

2. Claims 9-46 and 53-97 are pending.

3. Applicant's election with traverse of Group, XXXII, claims 66-67, now claims 66 - 68 and 93-97 in the reply filed on 01/27/05 and SEQ ID NO:1 as a species of INPROL and naloxone as species of opiate compound in the reply filed on 06/21/05 is acknowledged. Applicant traverse the Restriction Requirement on the grounds that the search of Groups XXXII and XXXI together would not constitute a serious search burden on the examiner and that search of the claims of Group XXXII would provide useful information for the claims of Group XXXI.

Applicant's arguments have been found persuasive the restriction requirement between groups XXXII and XXXI is hereby withdrawn. Upon further consideration the prior art search has been extended to include all species of INPROL, recited in claim 93 and all species of opiate compound recited in claim 68. The species election is hereby withdrawn.

Claims 9-46, 53-65 and 69-92 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 66-68 and 93-97 reads on a method of stimulating stem cell division in a mammal exposed to an agent which damage or destroys stem cells comprising administering a stimulating amounts of INPROL and/or opiate compound are under consideration in the instant application.

4. The specification on page 1, should be amended to reflect the status of the parent 08/832,443 application.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

6. The information disclosure statement filed 02/12/04 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.
International Search Reports on the IDS, filed 02/12/04 has been considered, however said citation has been crossed out as it is not appropriate for printing in an issued patent.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112.
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 93, 94, 96 and 97 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. In claims 93, 94, 96 and 97 the recitation of the peptide designated as SEQ ID NO:37 is unclear. The same peptide has been designated as SEQ ID NO:1 at page 21 of the instant specification. It is unclear which SEQ ID NO is correct.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 66, 67, 68 and 95 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of stimulating stem cell division in a mammal exposed to an agent which damages or destroys stem cells, comprising administering a stem cell proliferation stimulating amount of INPROL, wherein said INPROL is selected from the group recited in claim 93, does not reasonably provide enablement for a method of stimulating stem cell division in a mammal exposed to an agent which damages or destroys stem cells, comprising administering a stem cell proliferation stimulating amount of *any* INPROL as claimed in claims 66, 67, 68 and 95. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

The claims as written encompass the genus of INPROL polypeptide that can stimulate stem cell proliferation. The genus encompasses peptides wherein such peptides have numerous differences in amino acid sequences.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

Applicant disclosed the isolation and use for the method of stimulating stem cell proliferation only INPROL peptides and polypeptides as recited in claim 93 of the instant specification (see examples 12, 13, 14, 15 and 16 of the instant Specification in particular) Applicant has not taught and exemplified how to make and/or use *any* INPROL peptides or polypeptides for the method of stimulating stem cell proliferation, comprising administering stimulating amount of any INPROL The structural and functional characteristics of any IMPROL are not defined in the claim. Applicant has not provided sufficient biochemical information (e.g. structural characteristics, amino acid composition , physicochemical properties, etc) that distinctly identifies such "IMPROL " other than IMPROL peptides and polypeptides as recited in claim 93. While any IMPROL may have some notion of the activity of the IMPROL peptides and polypeptides as recited in claim 93 claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make and use such agents, commensurate in scope with the claimed invention. There is insufficient direction or objective evidence as to how to make and to how to use *any* INPROL peptide or polypeptide which after administering in a mammal can stimulate stem cell division for the number of possibilities associated with the myriad of direct and indirect effects associated with various INPROL peptide and polypeptide and, in turn, as to whether such a desired effect can be achieved or predicted, as encompassed by the claims.

Applicant is relying upon certain biological activities and the disclosure of a limited species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated *any* INPROL encompassed by the claimed invention other than INPROL peptides and polypeptides recited in claim 93 would be expected to have greater differences in their activities. Moreover, US Patent 6,022,848 (IDS) and WO 94/22915 (IDS) both teaches the existence of INPROL peptides that are an inhibitors of stem cell proliferation (see entire US Patent '848, column 4 in particular and entire WO' 915 page 7 in particular). Without sufficient guidance, the changes which can be made in the structure of *any* INPROL peptide or polypeptide and still provide or maintain sufficient or the claimed activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Since the instant fact pattern fails to indicate that representative number of structurally related compounds is disclosed, the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claims and consequently would not know how to make them. An assay for *finding* a product is not equivalent to a positive recitation of *how to make* a product.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method of stimulating stem cell division in a mammal exposed to an agent which damages or destroys stem cells, comprising administering a stem cell proliferation stimulating amount of *any* INPROL as claimed in claims 66, 67, 68 and 95 in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

12. Claims 66, 67, 68 and 95 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : a method of stimulating stem cell division in a mammal exposed to an agent which damages or destroys stem cells, comprising administering a stem cell proliferation stimulating amount of INPROL, wherein said INPROL is selected from the group recited in claim 93.

Applicant is not in possession of : a method of stimulating stem cell division in a mammal exposed to an agent which damages or destroys stem cells, comprising administering a stem cell proliferation stimulating amount of *any* INPROL as claimed in claims 66, 67, 68 and 95.

The claimed invention is drawn to a genus of INPROL polypeptide that can stimulate stem cell proliferation. The genus encompasses peptides wherein such peptides have numerous differences in amino acid sequences, however, structural identifying characteristics of the genus are not disclosed. There is no evidence that there is any *per se* structure/function relationship between the disclosed INPROL peptide and polypeptide and any others that might be found using the claimed method. The specification does not disclosed *any* INPROL that can be used in a method of stimulating stem cell division in a mammal exposed to an agent which damages or destroys stem cells. The Specification only disclosed INPROL as recited in claim 93, that

can be used in a method of stimulating stem cell division in a mammal exposed to an agent which damage or destroys stem cells.

Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of what a material does rather than of what it is, usually does not suffice. The patent does not more than describe the desired function of the compound called for and contains no information by which a person of ordinary skill in the art would understand that the inventors possessed the claimed invention. At best, it simply indicates that one should run tests on a wide spectrum of compounds in the hope that at least one of them will work. Inadequate written description that merely identifies a plan to accomplish an intended result "is an attempt to preempt the future before it has arrived" *Fiers v. Revel*, 984 F.2d 1164,1171 9Fed.Cir. 1993).

The Examiner notes that the claimed invention which is drawn to a genus of INPROL polypeptide sequences may be adequately described if there is a (1) sufficient description of a representative number of species, or (2) by disclosure of relevant, identifying characteristics sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. To satisfy the disclosure of a "representative number of species" will depend on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. "Relevant, identifying characteristics" include structure or other physical and /or chemical properties, functional characteristics coupled with a known or disclosed correlation between function and structure, or a combination of such identifying characteristics sufficient to show the applicant was in possession of the claimed genus. (see Revised Guidelines for the Examination of Patent Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 66-68 and 93-97 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,784155 in view of US Patent 6,280739.

Claims 1-15 of U.S. Patent No. '155 recite a method of stimulating stem cell proliferation comprising contacting hematopoietic cells with a stem cell proliferation stimulating amount of INPROL alone or in combination with proliferation stimulating amount of an opiate compound wherein INPROL is selected from the group recited in claims 1 and 3; or wherein opiate compound is selected from the group as recited in claim 6. It is noted that the same opiate compound and INTERPOL are recited in the instant claims.

Claims 1-15 of U.S. Patent No. '155 do not explicitly recited a method of stimulating stem cell division in a mammal exposed to an agent which damage or destroys stem cells comprising administering a stem cell proliferation stimulating amount of INPROL wherein said agent are antiviral or anti-neoplastic agent.

US Patent 739 teaches the method of stimulating stem cells proliferation, i.e. cell division the patients exposed to irradiation/chemotherapy or anti-viral or anti-cancer (i.e. anti-neoplastic) agent which destroys stem cells, comprising administering the proteins of the invention. US Patent 739 teaches that stimulation of stem cell division would be useful in restoring the hematopoietic and immune systems of a patient undergoing irradiation/chemotherapy or anti-viral or anti-cancer therapy (see entire document, overlapping columns 10 -14 in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of US Patent '739 to those recited in Claims 1-15 of U.S. Patent No. '155 to obtain a claimed method of stimulating stem cell division in a mammal exposed to an agent which damage or destroys stem cells comprising administering a stem cell proliferation stimulating amount of INPROL wherein said agent are antiviral or anti-neoplastic agent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do and so because stimulating stem cell division is useful for restoring the hematopoietic and immune systems of a patient undergoing irradiation/chemotherapy or anti-viral or anti-cancer therapy as taught by US Patent '739 and to substitute peptide taught by US Patent '739 with INPROL peptide or polypeptide that can stimulate stem cell proliferation as recited in claims 1-15 of U.S. Patent No. '155. Specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See CTS Com. v. Electro Materials Corp. of America 202 USPQ 22 (DC SINY); and In re Burckel 201 USPQ 67 (CCPA).

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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